Additional Baseline Data

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Additional Baseline Data

Tab. 1: Number of patients per study center

Center-No.	Patients	
	N	%
01	16	9.7
02	20	12.1
03	1	0.6
04	14	8.5
05	10	6.1
06	7	4.3
07	4	2.4
08	20	12.1
09	17	10.3
10	8	4.8
11	2	1.2
12	1	0.6
13	0	0.0
14	14	8.5
15	8	4.8
16	14	8.5
17	7	4.3
18	0	0.0
19	2	1.2
All	165	100.0

Number of patients per study center, patients were recruited in 17 centers

Tab. 2: Premature discontinuation of study

Premature discontinuation of study?	ALL	
	N	%
Yes	0	0.0
No	165	100.0
All	165	100.0

None of the patients dropped out

Tab. 3: Protocol deviations

Protocol deviation	Cohort								All			
	1st analysis sample				2nd analysis sample							
	Treatment				Treatment				Treatment			
	Placebo		Verum		Placebo		Verum		Placebo		Verum	
	N	%	N	%	N	%	N	%	N	%	N	%
No deviations	16	66.6	17	65.4	44	75.9	45	78.9	60	73.2	62	74.7
Minor deviations	8	33.3	9	34.6	13	22.4	12	21.1	21	25.6	21	25.3
Major deviations	.	.	.	.	1	1.7	.	.	1	1.2	.	.
All	24	100.0	26	100.0	58	100.0	57	100.0	82	100.0	83	100.0

Protocol deviations

Overall there were 20 cases (10 from placebo and 10 from verum treatment) with randomization errors, due to a misleading of randomization in ascending order. Additionally all patients of study center no. 2 (placebo group: n=10; verum group: n=10) had got a wrong patient number by mistake. Deviating from the protocol the study center combined the number of the study center and the randomization number to the patient number instead of the number of the study center and the number of patient at site in ascending order, starting with 1. All these deviations were regarded as “minor” violations, as they did not affect the primary efficacy variable. They did not led to an exclusion from study participation.

Furthermore 2 patients (1 from placebo and 1 from verum treatment) did not fulfil the exclusion criterion of medical reliable contraception:

Pat.-No.: 0510 where the partner had have a vasectomy and

Pat.-No.: 1410 where abstinence (“Enthaltsamkeit”) was stated.

These deviations were regarded as “minor” violations also. Therefore none of these patients were excluded from study participation, even though the respective exclusion criterion was answered with “yes” in the CRF.

Pat.-No. 1901 reported a pain intensity of only 4 points on the VRS (0-10) during the screening and did not fulfil the inclusion criteria of 5 points on the VRS in minimum. This deviation met one of the inclusion criteria. It was regarded as a “major” protocol deviation, which was not acceptable. Nevertheless the respective investigator randomized this patient, but answered the according inclusion criterion with “no”.

Tab. 4: Details on Protocol deviations

	OVERALL
Number of patients	165 (100.0%)
Inclusion criteria not fulfilled	
Not detected	164 (99.4%)
Yes	1 (0,6%)
Exclusion criteria present	
Not detected	163 (98.8%)
Yes	2 (1.2%)
Wrong co-medication	
Not detected	165 (100.0%)
Yes	0 (0.0%)
Treatment schedule violation	
Not detected	165 (100.0%)
Yes	0 (0.0%)
Randomization error	
Not detected	145 (87.9%)
Yes	20 (12.1%)
“Other” (incorrect patient number)	
Not detected	145 (87.9%)
Yes	20 (12.1%)

Tab. 5: Number of patients by type of protocol deviation - all randomized patients

	OVERALL
Number of patients	165 (100.0%)
Overall assessment of Protocol Deviations	
Fully acceptable	122 (73.9%)
Not acceptable	1 (0.6%)
Acceptable but deviations	42 (25.5%)
No study drug given	0 (0.0%)

Number of patients by overall assessment of protocol deviations - all randomized patients.
None of the patients took excluded or forbidden co-medication. Treatment schedule violations were not reported as well as no “other” protocol deviations.
Due to the fact that less than 5% of the patients were excluded from the FAS set, no PP analysis was performed,

Tab. 6: Patients in childbearing age

Childbearing age	Cohort								All			
	1st analysis sample				2nd analysis sample							
	Treatment				Treatment				Treatment			
	Placebo		Verum		Placebo		Verum		Placebo		Verum	
	N	%	N	%	N	%	N	%	N	%	N	%
No	2	25.0	1	8.3	7	17.1	10	32.3	9	18.4	11	25.6
Yes	6	75.0	11	91.7	34	82.9	21	67.7	40	81.6	32	74.4
All	8	100.0	12	100.0	41	100.0	31	100.0	49	100.0	43	100.0

Tab. 7: Effective contraception within childbearing aged group

Contraception	Cohort								All			
	1st analysis sample				2nd analysis sample							
	Treatment				Treatment				Treatment			
	Placebo		Verum		Placebo		Verum		Placebo		Verum	
	N	%	N	%	N	%	N	%	N	%	N	%
No	.		.	.	1	2.4	1	3.2	1	2.0	1	3.1
Yes	6	75.0	11	91.6	33	80.5	20	64.6	39	79.6	31	72.1
Condom	2	25.0	.	.	3	7.3	.	.	5	10.2	.	.
Coil	1	12.5	4	33.3	3	7.3	4	12.9	4	8.2	8	18.6
Sterilization	.	.	.	.	2	4.9	1	3.3	2	4.1	1	2.3
oral / hormonal	3	37.5	6	50.0	21	51.2	15	48.4	23	46.9	21	48.9
unknown	.	.	1	8.3	4	9.8	.	.	4	8.2	1	2.3

Demographic variables

Tab. 8: Age (years)

Age [Years]		Cohort				All	
		1st analysis sample		2nd analysis sample			
		Treatment		Treatment		Treatment	
		Placebo	Verum	Placebo	Verum	Placebo	Verum
	Mean	38.08	34.38	32.86	36.00	34.39	35.49
	Std	13.15	13.02	13.71	13.45	13.68	13.25
	Min	19.00	18.00	18.00	18.00	18.00	18.00
	Median	35.00	32.00	29.50	35.00	31.00	35.00
	Max	73.00	63.00	74.00	74.00	74.00	74.00

Tab. 9: Grouped Age

Age grouped	Cohort								All			
	1st analysis sample				2nd analysis sample							
	Treatment				Treatment				Treatment			
	Placebo		Verum		Placebo		Verum		Placebo		Verum	
	N	%	N	%	N	%	N	%	N	%	N	%
18 - <35 Years	12	50.0	14	53.8	36	62.1	27	47.4	48	58.5	41	49.4
35 - <45 Years	5	20.8	5	19.2	8	13.8	14	24.6	13	15.9	19	22.9
45 - <55 Years	5	20.8	5	19.2	10	17.2	12	21.1	15	18.3	17	20.5
55 - <65 Years	1	4.2	2	7.7	2	3.4	2	3.5	3	3.7	4	4.8
>= 65 Years	1	4.2	.	.	2	3.4	2	3.5	3	3.7	2	2.4
All	24	100.0	26	100.0	58	100.0	57	100.0	82	100.0	83	100.0

Tab. 10: Height and weight at baseline

Body measurements		Cohort				All	
		1st analysis sample		2nd analysis sample			
		Treatment		Treatment		Treatment	
		Placebo	Verum	Placebo	Verum	Placebo	Verum
Height [cm]	N	24	26	58	57	82	83
	Mean	175.13	173.50	169.12	170.58	170.88	171.49
	Std	10.14	7.90	8.19	10.11	9.16	9.52
	Min	152.00	162.00	154.00	150.00	152.00	150.00
	Median	175.00	172.50	168.50	170.00	169.00	171.00
	Max	190.00	192.00	198.00	192.00	198.00	192.00
Weight [kg]	N	24	26	58	57	82	83
	Mean	78.75	70.00	71.48	74.60	73.61	73.16
	Std	20.09	13.32	12.68	18.88	15.46	17.39
	Min	42.00	53.00	46.00	49.00	42.00	49.00
	Median	76.50	69.00	71.50	71.00	72.00	71.00
	Max	122.00	93.00	100.00	126.00	122.00	126.00

Tab. 11: Ethnic origin

Ethnic origin	Cohort								All			
	1st analysis sample				2nd analysis sample							
	Treatment				Treatment				Treatment			
	Placebo		Verum		Placebo		Verum		Placebo		Verum	
	N	%	N	%	N	%	N	%	N	%	N	%
Caucasian	24	100.0	26	100.0	57	98.3	56	98.2	81	98.8	82	98.8
Other (asian)	.	.	.	.	1	1.7	1	1.8	1	1.2	1	1.2
All	24	100.0	26	100.0	58	100.0	57	100.0	82	100.0	83	100.0

Tab. 12: Number of patients with any medical history at screening

Any relevant medical history?	Cohort								All			
	1st analysis sample				2nd analysis sample							
	Treatment				Treatment				Treatment			
	Placebo		Verum		Placebo		Verum		Placebo		Verum	
	N	%	N	%	N	%	N	%	N	%	N	%
Not applicable	1	4.2	.	.	1	1.7	.	.	2	2.4	.	.
No	9	37.5	12	46.2	22	37.9	28	49.1	31	37.8	40	48.2
Yes	14	58.3	14	53.8	35	60.3	29	50.9	49	59.8	43	51.8
All	24	100.0	26	100.0	58	100.0	57	100.0	82	100.0	83	100.0

As demanded by one of the exclusion criteria, treatment with analgesics/ non-steroidal anti-inflammatory drugs (NSAIDs), cortisone and cortisone derivatives, antiphlogistics, oropharyngeal therapeutics, anticonvulsants or psychotropics within 24 hours prior to enrolment was not given for any patient. Furthermore no treatment with slow-acting non-steroidal anti-inflammatory drugs (NSAIDs) within 10 days prior to enrolment and treatment with antibiotics within 14 days prior to enrolment, was reported.

Tab. 13: Number of patients with prior medication

Any prior medication?	Cohort								All			
	1st analysis sample				2nd analysis sample							
	Treatment				Treatment				Treatment			
	Placebo		Verum		Placebo		Verum		Placebo		Verum	
	N	%	N	%	N	%	N	%	N	%	N	%
Not applicable	.	.	.	.	1	1.7	.	.	1	1.2	.	.
No	11	45.8	12	46.2	17	29.3	26	45.6	28	34.1	38	45.8
Yes	13	54.2	14	53.8	40	69.0	31	54.4	53	64.6	45	54.2
All	24	100.0	26	100.0	58	100.0	57	100.0	82	100.0	83	100.0

First sample: A total number of 13 patients (54.2%) in the placebo group used medication during the last 3 months before the screening visit. In the verum group prior medication was used by 14 patients (53.8 %).
Second sample: With respect to the second analysis sample it was reported that a number of 40 (69.0%) patients in the placebo group and 31 patients (54.4%) in the verum group used prior medication.

Physical examination

Tab. 14: Number of patients with abnormal findings in physical examination at screening

Physical examination	Cohort								All			
	1st analysis sample				2nd analysis sample							
	Treatment				Treatment				Treatment			
	Placebo		Verum		Placebo		Verum		Placebo		Verum	
	N	%	N	%	N	%	N	%	N	%	N	%
Normal	17	70.8	20	76.9	40	69.0	43	75.4	57	69.5	63	75.9
Abnormal	7	29.2	6	23.1	18	31.0	14	24.6	25	30.5	20	24.1
All	24	100.0	26	100.0	58	100.0	57	100.0	82	100.0	83	100.0

Tab. 15: Number of patients with abnormal physical examination findings at screening by organ/body system

Physical examination		Cohort								All			
		1st analysis sample				2nd analysis sample							
		Treatment				Treatment				Treatment			
		Placebo		Verum		Placebo		Verum		Placebo		Verum	
		N	%	N	%	N	%	N	%	N	%	N	%
General	Abnormal without relevance	.	.	.	.	6	10.3	4	7.0	6	7.3	4	4.8
Skin	Abnormal without relevance	3	12.5	2	7.7	2	3.4	5	8.8	5	6.1	7	8.4
Eyes, ears and nose	Abnormal without relevance	1	4.2	1	3.8	.	.	3	5.3	1	1.2	4	4.8
	Abnormal with relevance	.	.	.	.	3	5.2	1	1.8	3	3.7	1	1.2
Head and neck	Abnormal without relevance	2	8.3	3	11.5	3	5.2	4	7.0	5	6.1	7	8.4
Lung	Abnormal without relevance	.	.	.	.	.	.	.	.	.	.	.	.
Heart	Abnormal without relevance	.	.	.	.	1	1.7	.	.	1	1.2	.	.
Abdomen	Abnormal without relevance	1	4.2	.	.	3	5.2	1	1.8	4	4.9	1	1.2
Lymph nodes	Abnormal without relevance	3	12.5	2	7.7	.	.	1	1.8	3	3.7	3	3.6
Musculoskeletal	Abnormal without relevance	5	20.8	6	23.1	6	10.3	5	8.8	11	13.4	11	13.3
	Abnormal with relevance	.	.	.	.	1	1.7	.	.	1	1.2	.	.
Neurologic	Abnormal without relevance	1	4.2	2	7.7	2	3.4	1	1.8	3	3.7	3	3.6
Other	abnormal without relevance	.	.	1	3.8	4	6.9	3	5.3	4	4.9	4	4.8

Vital signs

Tab. 16: Vital signs – systolic, diastolic blood pressure and pulse rate at baseline

Vital signs		Cohort				All	
		1st analysis sample		2nd analysis sample			
		Treatment		Treatment		Treatment	
		Placebo	Verum	Placebo	Verum	Placebo	Verum
Systolic BP [mm HG]	N	24	26	58	57	82	83
	Mean	125.25	120.23	118.38	124.35	120.39	123.06
	Std	11.60	12.04	12.53	11.37	12.60	11.67
	Min	110.00	100.00	94.00	99.00	94.00	99.00
	Median	120.00	120.00	115.00	120.00	120.00	120.00
	Max	155.00	148.00	150.00	158.00	155.00	158.00
Diastolic BP [mm HG]	N	24	26	58	57	82	83
	Mean	77.88	74.96	76.86	77.53	77.16	76.72
	Std	10.19	7.02	9.14	5.60	9.41	6.15
	Min	60.00	65.00	60.00	68.00	60.00	65.00
	Median	80.00	73.00	80.00	80.00	80.00	78.00
	Max	95.00	90.00	98.00	90.00	98.00	90.00
Pulse [beats/min]	N	24	26	58	57	82	83
	Mean	74.00	72.04	72.02	73.63	72.60	73.13
	Std	7.92	8.19	8.75	9.64	8.52	9.19
	Min	58.00	55.00	59.00	59.00	58.00	55.00
	Median	72.00	73.00	72.00	72.00	72.00	72.00
	Max	92.00	88.00	100.00	129.00	100.00	129.00

Tab. 17: Pain intensity (VRS 0-10) at baseline (sample 1, N=50)

Pain intensity (VRS 0-10) at baseline		Treatment		All
		Placebo	Verum	
	N	24	26	50
	Median	7.0	7.0	7.0
	Min	5.0	5.0	5.0
	Q1	6.0	6.0	6.0
	Q3	7.0	8.0	8.0

Tab. 18: Pain intensity (VRS 0-10) at baseline (sample 2, N=115)

Pain intensity (VRS 0-10) at baseline		Treatment		All
		Placebo	Verum	
	N	58	57	115
	Median	7.0	7.0	7.0
	Min	4.0	5.0	4.0
	Q1	6.0	6.0	6.0
	Q3	8.0	8.0	8.0
	Max	10.0	10.0	10.0
	Mean	7.0	6.9	7.0
	Std	1.5	1.3	1.4

Tab. 19: Pain intensity (VRS 0-10) at baseline (combined sample, N=165)

Pain intensity (Likert-scale) at baseline		Treatment		All
		Placebo	Verum	
	N	82	83	165
	Median	7.0	7.0	7.0
	Min	4.0	5.0	4.0
	Q1	6.0	6.0	6.0
	Q3	8.0	8.0	8.0
	Max	10.0	10.0	10.0
	Mean	6.9	7.0	7.0
	Std	1.3	1.2	1.3